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The Effects of Low Frequency Electromagnetic Fields on the Melatonin Synthesis in Man

Barbara Griefahn, Gisela Degen, Meinolf Blaszkewicz,
Klaus Golka, Christa Künemund, Ricarda Their

Prof. Dr. Barbara Griefahn
Institute for Occupational Physiology (Institut für Arbeitsphysiologie)
at the University of Dortmund
Ardeystr. 67, D-44139 Dortmund, Germany
Phone: +49 231 1084 221
Fax: +49 231 1084 400
email: griefahn@arb-phys.uni-dortmund.de

Melatonin – synthesis and functions

Some studies (mainly in rodents) have raised concerns regarding a carcinogenic potential of low-frequency electric and/or magnetic fields which may be related to the inhibition of melatonin synthesis. This hormone – isolated by Lerner et al. in 1958 [14] – is thought to exert an oncostatic effect probably by acting as a free radical scavenger [20, 21, 22]. The chronobiological properties of melatonin are much better founded. Melatonin mediates the entrainment (synchronization) of the periodic diurnal alterations of physiologic functions (core temperature, heart rates etc. [2, 4]). Moreover, melatonin has probably numerous other functions which are as yet insufficiently studied (thermoregulation, cardiovascular and immune functions etc.) [6, 7].

Circadian rhythm of melatonin synthesis: Without any time cues, the synthesis of melatonin follows an endogenous circadian rhythm with a period of about 25 hours on the average. The rhythm is controlled by the endogenous pacemaker which is located in the suprachiasmatic nucleus and entrained by the light-dark cycle to a diurnal 24-hours rhythm. The information about the light is transmitted from the retina to the endogenous pacemaker and then via several neurons to the pineal gland, where the synthesis of melatonin is inhibited [3, 12]. The synthesis starts with or after the onset of dark and decreases in the early morning. So, the actual concentration of melatonin reveals a distinct diurnal rhythm.

The onset of melatonin synthesis, the time and the amplitude of its maximum varies considerably between individuals but is rather stable for an individual [1, 3, 8, 9, 26].

Inhibition of melatonin synthesis by electromagnetic waves: Apart from natural light, the synthesis of melatonin is also inhibited by artificial light where the extents of the effects depend on intensity and wavelength as well as on the time and the duration of exposure [2, 10]. Similar, though far smaller effects were evoked in animal experiments by other parts of the electromagnetic spectrum, namely by UV-A radiation (320-400 nm) [5, 19] and by low-frequency magnetic fields [26]. A similar effect may be evoked by thermal radiation as well.

Effects of low-frequency magnetic fields on melatonin synthesis

Animal experiments have unequivocally revealed an inhibititory effect of low-frequency magnetic fields on the synthesis of melatonin. Magnetic fields are presumably perceived as well as light by the photoreceptors of the retina, thus

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suggesting the same underlying mechanism [e.g. 11, 13, 17, 27].

These effects are debated for human beings. Pfluger and Minder [18] observed that railway workers who were exposed during their shifts to magnetic fields (16.7 Hz, 20 μT on the average) excreted less 6-hydroxymelatonin sulfate. But these results are not convincing as the respective workers were also exposed to light during their duties.

Wilson et al. [25] registered a reduced excretion of 6-hydroxymelatonin sulfate in some of their subjects who slept with an electrically heated blanket. Schiffmann et al. [23] observed 8 subjects during a control night without any exposure and during 2 nights with exposure to a magnetic field or to bright light, respectively, between 1 a.m. and 2 a.m.. Actual plasma concentration of melatonin was, however, exclusively reduced after exposure to light.

Selmaoui et al. [24] observed 16 subjects (20-30 yrs) during two 24 h periods. Following a standardized protocol during the day (8 a.m. to 11 p.m.) the subjects were then exposed during the night to a continuous or to an intermittent magnetic field, respectively (50 Hz, 10 μT). Actual plasma concentration of melatonin was determined every hour and the excretion of 6-hydroxymelatonin sulfate over consecutive 3-hour periods. Melatonin production was not influenced compared to a control group comprizing another 16 subjects.

Wood et al. [26] determined a window of temporal sensitivity. In their experiments melatonin synthesis was only suppressed when magnetic fields (50 Hz, 20 μT) were applied before and during the onset of melatonin production in the evening which was determined during a 'baseline night' without any exposure to magnetic fields.

Graham et al. [8, 9] conducted 3 studies, where the subjects were studied first in two control nights to determine the individual basic melatonin production and the individual reaction to light. Basic melatonin production was indicated by a single blood sample taken at 2 a.m. and the effect of light was determined by the difference of plasma concentrations before and after a 1-hour exposure (5 500 lux, 2 a.m to 3 a.m.). During the 3rd night every third subject slept under the influence of an intermittent 60 Hz magnetic field of 2 or 20 μT, respectively or without any exposure (control group). Actual plasma concentration of melatonin was determined every hour. In the first study, subjects with a low level of melatonin revealed a significantly greater inhibition of melatonin synthesis due to light as well as to the stronger magnetic field (20 μT). In both the following studies this result was not replicated. Though carefully executed these 3 studies reveal nevertheless some methodological errors.

- The single determination of melatonin concentration at 2 a.m. does not take into account the considerable differences in the temporal distribution of melatonin synthesis between subjects. Reliable information on basal melatonin production would have required an hourly sampling as it was done in the experimental nights. Thus, the subsequent categorization of an individual's melatonin production is at least questionable.
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- The restriction of the observation period to the duration of sleep and exposure neglects a possible rebound, which would have required an extension of the sampling period [10].
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- Due to the great differences between subjects a within subject comparison would have been advisable, i.e. sham versus field exposure.

The assumption that individuals react differently to electromagnetic waves (light, magnetic fields) is plausible and the consequences are relevant not only for work. The confirmation of a greater reduction of melatonin synthesis in persons with habitually low melatonin synthesis would imply that particularly babies during the first weeks of life, old people and presumably persons with a late circadian phase (evening types) are affected.

Methods

This study which was started some weeks ago aims to investigate experimentally the effects of extremely low-frequency magnetic fields on the synthesis of melatonin in man. The following requirements are fulfilled:

- within subjects comparisons which presuppose identical procedures during control- and during exposure nights
- frequent (hourly) determination of actual melatonin concentration (saliva)
- observation periods must exceed exposure time to detect rebound effects
- control experiments without any exposure and with exposure to a stimulus with well known effects on melatonin synthesis (light) are advisable.
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As the actual individual phase might be important, masking effects are avoided by the application of constant routines [15].

Experimental design: The subjects are observed 4 times at weekly intervals for 24-hour periods. Regarding a permuted sequence the exposures listed in the table are planned.

	EMF	Light	Thermal radiation
Control	-	< 50 lux	18 °C
Magnetic field	16.7 Hz, 0.2 mT	< 50 lux	18 °C
Light	-	1 500 lux	18 °C
Thermal radiation	-	< 50 lux	t_r: 65 °C, t_a: 18 °C

The study concerns extremely low-frequency magnetic fields that are emitted by railways (16.7 Hz), to which many persons are regularly and frequently exposed. These are residents living along railway tracks, commuters who are periodically exposed twice a day and the employees of railway companies who are affected during their duties.

Technical equipment: the experiments are executed in 3 rooms, particularly designed and equipped for the respective purpose.
Control experiment and exposure to magnetic fields: The respective observations take place in a sound proofed room with an area of 2.80 m x 3.80 m, where two Helmholtz-coils with a diameter of 1.80 m each are located. The coil-to-coil distance is 92 cm, so that the subjects lie in a horizontally directed homogenuous field. The equipment is particularly designed for low frequency fields.

Thermal radiation: Exposure to thermal radiation takes place in a climatic chamber where radiation temperature (t_r), air temperature (t_a), humidity (RH) and air velocity (v_a), can be varied in a large range and adjusted precisely (t_a: - 35 to + 80 °C, t_r: t_a to + 200 °C, RH: 5 to 99 %, v_a: 0.1 to 4.5 m/s).

Light: Light exposure is realized in another climatic chamber which has the same specifications as the chamber used for radiation exposure. Light can be adjusted up to about 3 000 lux.

Apart from the respective exposure conditions air temperature is adjusted to 18 °C, the irradiance to less than 50 lux and the sound pressure level to 50 dBA (due to air conditioning).

In all these rooms the subjects can get into contact with the experimenter via an intercom system at any time.

Experimental procedure: After their arrival in the institute the subjects assess their actual health state and well-being. They then state their alcohol and drug consumption within the preceding 12 hours. In case of serious disturbances the experiments are postponed to another day.

After the application of the sensors (thermocouples for rectal temperature, electrodes for EKG) the subjects spend 24 hours in bed (noon to noon). Exposure (field, radiation, light) starts at 6 p.m. and is terminated at 2 a.m.. The subjects receive hourly small snacks (200 to 400 kJ). The plate is removed after 30 minutes as the subjects are not allowed to eat during the 30 minutes which preceed the collection of the saliva. So, the experimenters enter the experimental chambers every 30 minutes.

Biochemical, physiological and psychological measurements

Personal characteristics: When the subjects are introduced to the experiments, personal characteristics are determined with the 'Freiburger Personal Inventory'.

Subjective reactions: Immediately after having entered the experimental room and just before leaving the subjects fill in a short questionnaire, where they – using analogue scales – assess their actual mood, tension, tiredness etc..

Actual melatonin concentration: Actual concentration of salivary melatonin are determined hourly.

Actimetry: During observation time body movements are registered using actimeters that are tied to the wrists of the subjects. They allow the reliable detection of body movements, i.e. phases of different physical activity.

Core temperature: Rectal temperature is measured with thermistors (YSI 427 Yellow Springs) continuously 10 cm beyond the sphincter and stored as averages over each consecutive minute.

Heart rates: The electrocardiogram is registered continuously and stored to calculate heart rate variability.

Subjects: Altogether 12-16 healthy male subjects, aged 18 to 30 years are examined. As the individual melatonin synthesis is presumably associated with the individual circadian phase (morning-, evening types), the subjective circadian phase (SCP) [16] is determined with a questionnaire that proved to be a reliable instrument for this purpose.

Exclusion of subjects: Subjects suffering from chronic, particularly from cerebral diseases or having psychic alterations are not allowed to participate. This is verified by questionnaires.

Break-off criteria: The experiments are terminated on request of the subjects. Further break-off criteria are not foreseen.
At present, the data of alltogether 5 subjects are collected, however, not yet evaluated.

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